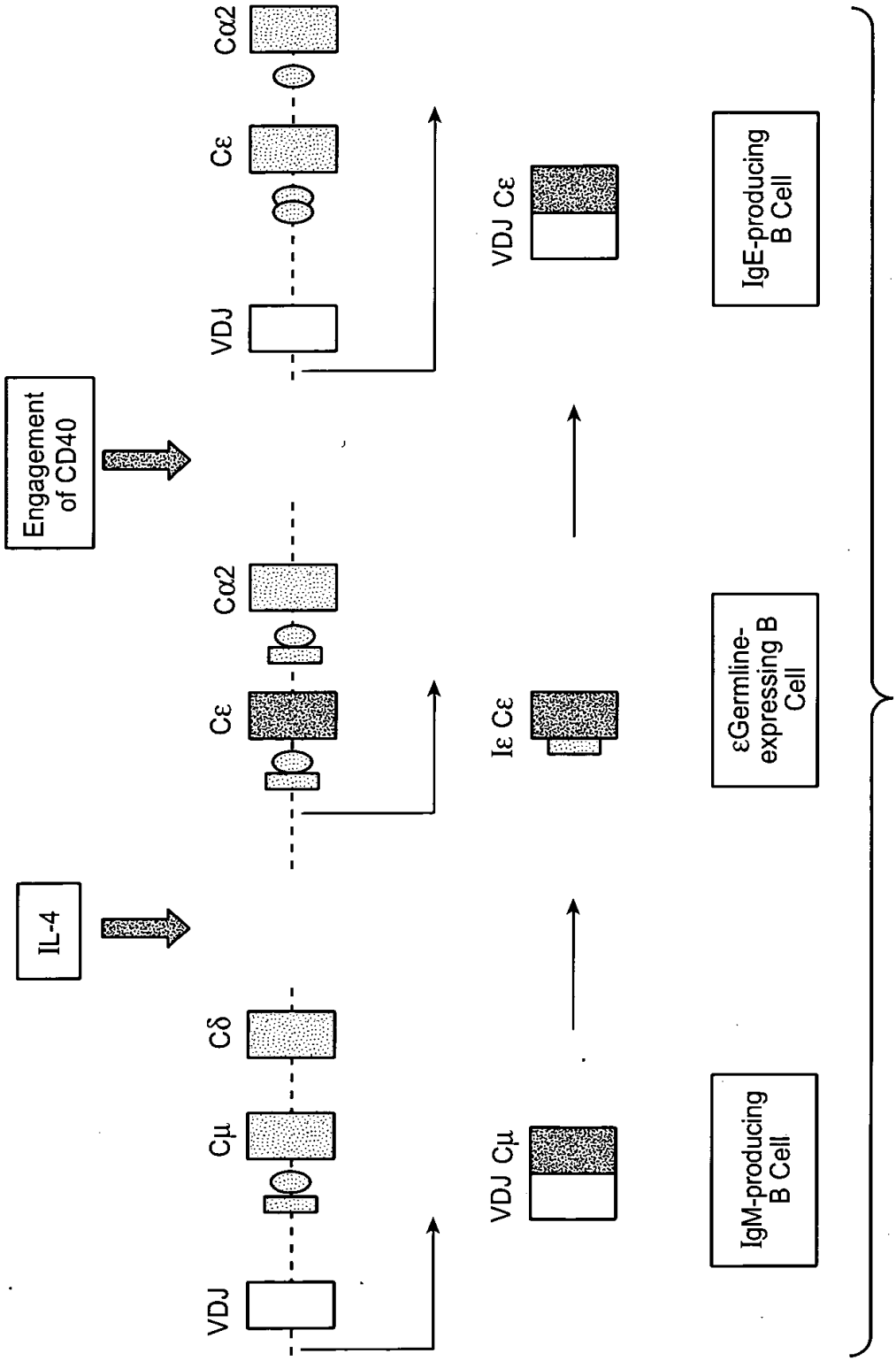
IL-4
Engagement of CD40
VDJ
Cμ
Cδ
VDJ Cμ
IgM-producing B Cell
Cε
Cα2
Iε Cε
εGermline-expressing B Cell
VDJ
Cε
Cα2
VDJ Cε
IgE-producing B Cell

FIG._1

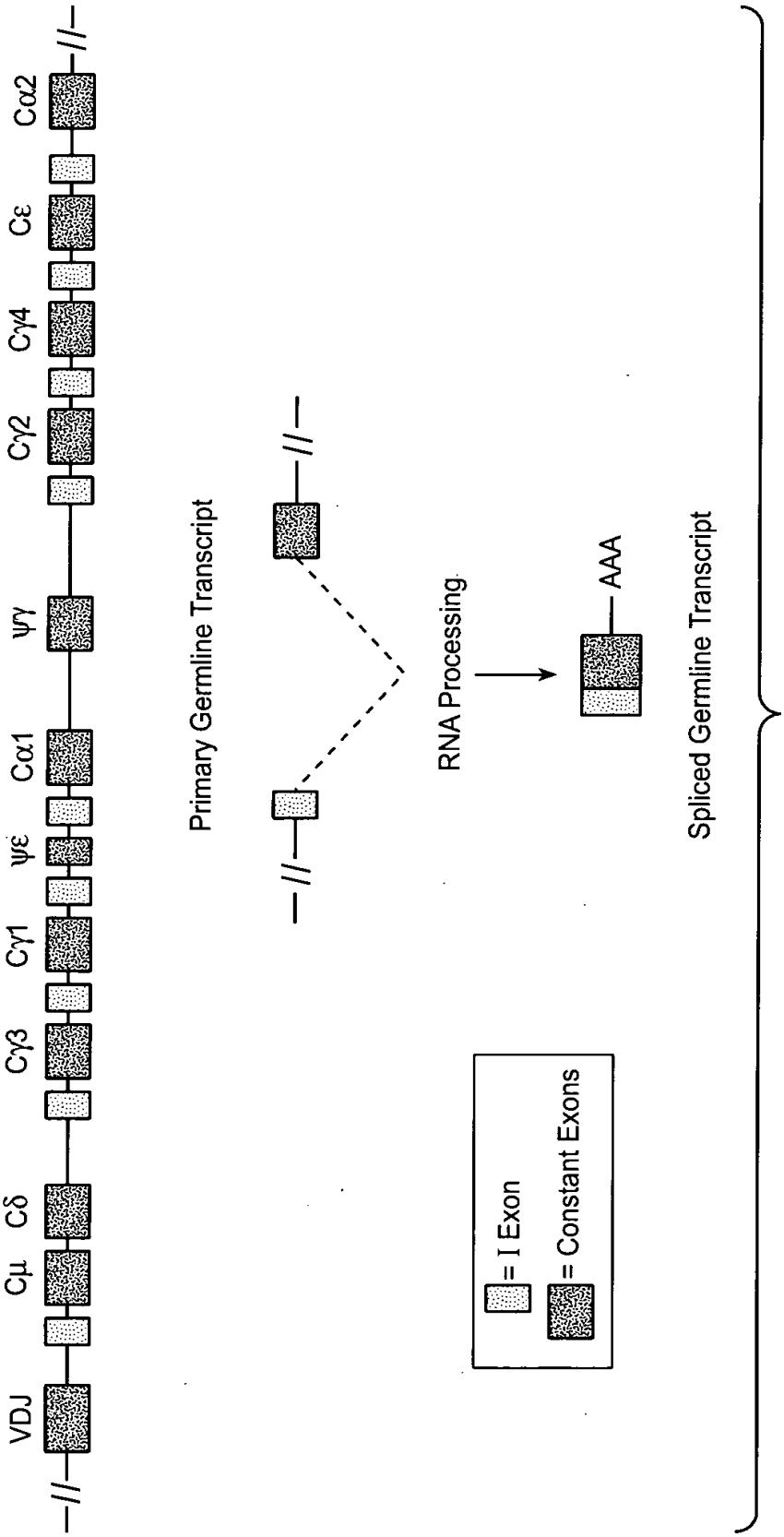
VDJ
Cμ
Cδ
Cγ3
Cγ1
ψε
Cα1
ψγ
Cγ2
Cγ4
Cε
Cα2
Primary Germline Transcript
RNA Processing
AAA
= I Exon
= Constant Exons
Spliced Germline Transcript

FIG._2

Germline Ig Alpha-2 Probe

CTCTGCTAAGGACAGACGGCCATCAAGGCAGGACCTGGGCCGGGCCAGGGCTCCCTCCCCACAGCAGCCCTCTTGGCAGG
CAGCCAGACGCCCGTGAGGGTGGACCTGCCATGAGGGCCTGCACGCCGGAGGCCGCCCACTCAGCACTGCGGGCCCTCCA
GCAGCCTGACCAGCATCCCCGACCAGCCCCAAGGTCTTCCCGCTGAGCCTCGACAGCACCCCCCAAGATGGGAACGTGGT
CGTCGCATGCCTGGTCCAGGGCTTCTTCCCCCAGGAGCCACTCAGTGTGACCTGGAGCGAAAGCGGACAGAACGTGACCG
CCAGAAACTTCCCACCTAGCCAGGATGCCTCCGGGGACCTGTACACCACGAGCAGCCAGCTGACCCTGCCGGCCACACAG
TGCCCAGACGGCAAGTCCGTGACATGCCACGTGAAGCACTACACGAATCCCAGCCAGGATGTGACTGTGCCCTGCCCAGT
TCCCCCACCTCCCCCATGCTGCCACCCCCGACTGTCGCTGCACCGACCGGCCC

Germline Ig Epsilon Probe

GGCTCCACTGCCCGGCACAGAAATAACAACCACGGTTACTGATCATCTGGGAGCTGTCCAGGAACCCGACAGGGAGCCGG
ACGGGCCACACCATCCACAGGCACCAAATGGACGACCCGGCGCTTCAGCCTCCACACAGAGCCCATCCGTCTTCCCCTTG
ACCCGCTGCTGCAAAAACATTCCCTCCAATGCCACCTCCGTG

Germline Ig Gamma 1 Probe

ACACACCAGAGGCTGACTGAGGCCTCCAGGACGACCGGGCTGGGAGCACGAGGAACATGACTGGATGCGGCAGAGCCGGC
CGTGGGGTGATGCCAGGATGGGCACGACCGACCTGAGCTCAGGAGGCAGCAGAGCGAGGGAGGAGGAGAGGCCCCAGGTG
AACGGAGGGGCTTGTCCAGGCCGGCAGCATCACCGGAGCCCAGGGCAGGGTCAGCAGTGCTGGCCGTGGGGCCCTCCTCT
CAGCCAGGACCAAGGACAGCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGG
GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGA
CCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC
AGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCC
CAAATCTTGTGACAAAACTCACACATGCCCACCG

FIG._3A

Germline Ig Gamma 2 Probe

CCAAGCCAACAGGGCAGGACACACCAGAGGCTGACTGAGGCCTCCATGACGACCAGGCTGGGAGCACGAGGAACATGACG
GGATGCGGCAGAGCCGGCCGTGGGGTGATGCCAGCATGGGCAGGACCCACCTGAGCTGAGGAGGCAGTAGAACGAGGGAG
GAGGAGAGGCCCCAGGTGAACGGAGGGGCTTGTCCAGGCCAGCAGCATCACTGGAGCCCAGGGCAGGGTCAGCAGTGCTG
GCCGTGGGGCCCTCTCTCAGCCAGGACCAAGGACAGCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCGCCCTGC
TCCAGGAGCACCTCCGAGAGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTG
GAACTCAGGCGCTCTGACCAGCGGCGTGCACACCTTCCCAGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCG
TGGTGACCGTGCCCTCCAGCAACTTCGGCACCCAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAACACCAAGGTG
GACAAGACAGTTGAGCGCAAATGTTGTGTCGAGTGCCCACCGTGCCCAGCACCACCTGTGGCAGGACCGTCA

Germline Ig Gamma 3 Probe

ACACACCAGAGGCTGACTGAGGCCTCCAGGACGACCGGGCTGGGAGCGTGAGGAACATGACGGGATGGGGCAGAGCCAGC
CATGGGGTGATGCCAGGATGGGCATGACCGACCTGAGCTCAGGAGGCAGCAGAGAGAGGGAGGAGGAGAGGCCCCAGGTG
AACCGAGGGGCTTGTCCAGGCCGGCAGCATCACCGGAGCCCAGGGCAGGGTCAGCAGAGCTGGCCGTAGGGCCCTCCTCT
CAGCCAGGACCAAGGACAGCAGCTTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCTGG
GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGA
CCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC
AGCAGCTTGGGCACCCAGACCTACACCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCT
CAAAACCCCACTTGGTGACACAACTCACACATGCCCACGGTGCCCAGAGCCCAAATCTTGTGACACACCTCCCCCGTGCC
CACGGTGCCC

Germline Ig Gamma 4 Probe

GGCCAGCACCACATGGAAGCCCAAGCGGAGCCAGCACGGGGGAGGTGGGCAGCCTTCAGGCACTGATGCCCACCCAGTGC
GAGACGACGGGGACCGTGGGCAGGGGCTTCCAAGCCAACAGGGCAGGACACACCAGAGGCTGACTGAGGCCTCCAGGACG
ACCGGGCTGGGAGCACGAGGAACATGACGGGATGCGGCAGAACCGGCCGTGGGGTGATGCCAGGATGGGCACGACCGACC
TGAGCTCAGGAGGCAGCAGAGCGAGGGAGGAGGAGAGGCCCCAGGTGAACGGAGGGGCTTGTCCAGGCCGGCAGCATCAC
CAGAGCCCAGGGCAGGGTCAGCAGAGCTGGCCGTAGGGCCCTCCTCTCAGCCAGGACCAAGGACAGCAGCTTCCACCAAG
GGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAAGGA
CTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTAC
AGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAAC
GTAGATCACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCGTC

FIG._3B

Germline Ig Alpha-1 Probe

GGCCTGGGCCGGGCCAGGGCTCCCTCCCCACAGCAGCCCTCTTGGCAGGCAGCCAGACGCCCGTGAGGGTGGACCTGCCA
TGAGGGCCTGCACGCCGGAGGCCGCCCACTCAGCACTGCGGGCCCTCCAGCAGCCTGACCAGCATCCCCGACCAGCCCCA
AGGTCTTCCCGCTGAGCCTCTGCAGCACCCAGCCAGATGGGAACGTGGTCATCGCCTGCCTGGTCCAGGGCTTCTTCCCC
CAGGAGCCACTCAGTGTGACCTGGAGCGAAAGCGGACAGGGCGTGACCGCCAGAAACTTCCCACCCAGCCAGGATGCCTC
CGGGGACCTGTACACCACGAGCAGCCAGCTGACCCTGCCGGCCACACAGTGCCTAGCCGGCAAGTCCGTGACATGCCAC

Germline Ig Alpha-2 Probe

CTCTGCTAAGGACAGACGGCCATCAAGGCAGGACCTGGGCCGGGCCAGGGCTCCCTCCCCACAGCAGCCCTCTTGGCAGG
CAGCCAGACGCCCGTGAGGGTGGACCTGCCATGAGGGCCTGCACGCCGGAGGCCGCCCACTCAGCACTGCGGGCCCTCCA
GCAGCCTGACCAGCATCCCCGACCAGCCCCAAGGTCTTCCCGCTGAGCCTCGACAGCACCCCCCAAGATGGGAACGTGGT
CGTCGCATGCCTGGTCCAGGGCTTCTTCCCCCAGGAGCCACTCAGTGTGACCTGGAGCGAAAGCGGACAGAACGTGACCG
CCAGAAACTTCCCACCTAGCCAGGATGCCTCCGGGGACCTGTACACCACGAGCAGCCAGCTGACCCTGCCGGCCACACAG
TGCCCAGACGGCAAGTCCGTGACATGCCAC

Germline Ig Epsilon Probe

GGCTCCACTGCCCGGCACAGAAATAACAACCACGGTTACTGATCATCTGGGAGCTGTCCAGGAACCCGACAGGGAGCCGG
ACGGGCCACACCATCCACAGGCACCAAATGGACGACCCGGCGCTTCAGCCTCCACACAGAGCCCATCCGTCTTCCCCTTG
ACCCGCTGCTGCAAAAACATTCCCTCCAATGCCACCTCCGTG

Germline Ig Gamma 1 Probe

ACACACCAGAGGCTGACTGAGGCCTCCAGGACGACCGGGCTGGGAGCACGAGGAACATGACTGGATGCGGCAGAGCCGGC
CGTGGGGTGATGCCAGGATGGGCACGACCGACCTGAGCTCAGGAGGCAGCAGAGCGAGGGAGGAGGAGAGGCCCCAGGTG
AACGGAGGGGCTTGTCCAGGCCGGCAGCATCACCGGAGCCCAGGGCAGGGTCAGCAGTGCTGGCCGTGGGGCCCTCCTCT
CAGCCAGGACCAAGGACAGCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGG
GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG

FIG._4A

Germline Ig Gamma 2 Probe

CCAAGCCAACAGGGCAGGACACACCAGAGGCTGACTGAGGCCTCCATGACGACCAGGCTGGGAGCACGAGGAACATGACG
GGATGCGGCAGAGCCGGCCGTGGGGTGATGCCAGCATGGGCAGGACCCACCTGAGCTGAGGAGGCAGTAGAACGAGGGAG
GAGGAGAGGCCCCAGGTGAACGGAGGGGCTTGTCCAGGCCAGCAGCATCACTGGAGCCCAGGGCAGGGTCAGCAGTGCTG
GCCGTGGGGCCCTCTCTCAGCCAGGACCAAGGACAGCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCGCCCTGC
TCCAGGAGCACCTCCGAGAGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG

Germline Ig Gamma 3 Probe

ACACACCAGAGGCTGACTGAGGCCTCCAGGACGACCGGGCTGGGAGCGTGAGGAACATGACGGGATGGGGCAGAGCCAGC
CATGGGGTGATGCCAGGATGGGCATGACCGACCTGAGCTCAGGAGGCAGCAGAGAGAGGGAGGAGGAGAGGCCCCAGGTG
AACCGAGGGGCTTGTCCAGGCCGGCAGCATCACCGGAGCCCAGGGCAGGGTCAGCAGAGCTGGCCGTAGGGCCCTCCTCT
CAGCCAGGACCAAGGACAGCAGCTTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCTGG
GGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAG

Germline Ig Gamma 4 Probe

GGCCAGCACCACATGGAAGCCCAAGCGGAGCCAGCACGGGGGAGGTGGGCAGCCTTCAGGCACTGATGCCCACCCAGTGC
GAGACGACGGGGACCGTGGGCAGGGGCTTCCAAGCCAACAGGGCAGGACACACCAGAGGCTGACTGAGGCCTCCAGGACG
ACCGGGCTGGGAGCACGAGGAACATGACGGGATGCGGCAGAACCGGCCGTGGGGTGATGCCAGGATGGGCACGACCGACC
TGAGCTCAGGAGGCAGCAGAGCGAGGGAGGAGGAGAGGCCCCAGGTGAACGGAGGGGCTTGTCCAGGCCGGCAGCATCAC
CAGAGCCCAGGGCAGGGTCAGCAGAGCTGGCCGTAGGGCCCTCCTCTCAGCCAGGACCAAGGACAGCAGCTTCCACCAAG
GGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAAGGA
CTACTTCCCCGAACCGG

FIG._4B

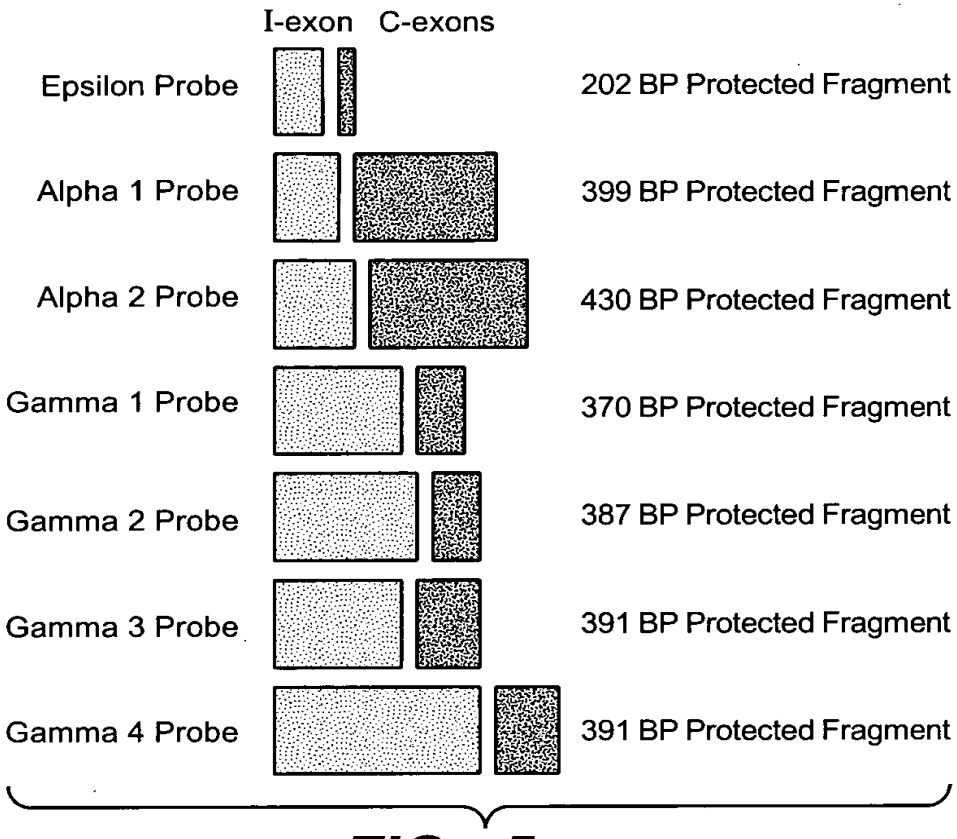
I-exon
C-exons
Epsilon Probe
202 BP Protected Fragment
Alpha 1 Probe
399 BP Protected Fragment
Alpha 2 Probe
430 BP Protected Fragment
Gamma 1 Probe
370 BP Protected Fragment
Gamma 2 Probe
387 BP Protected Fragment
Gamma 3 Probe
391 BP Protected Fragment
Gamma 4 Probe
391 BP Protected Fragment

FIG._5

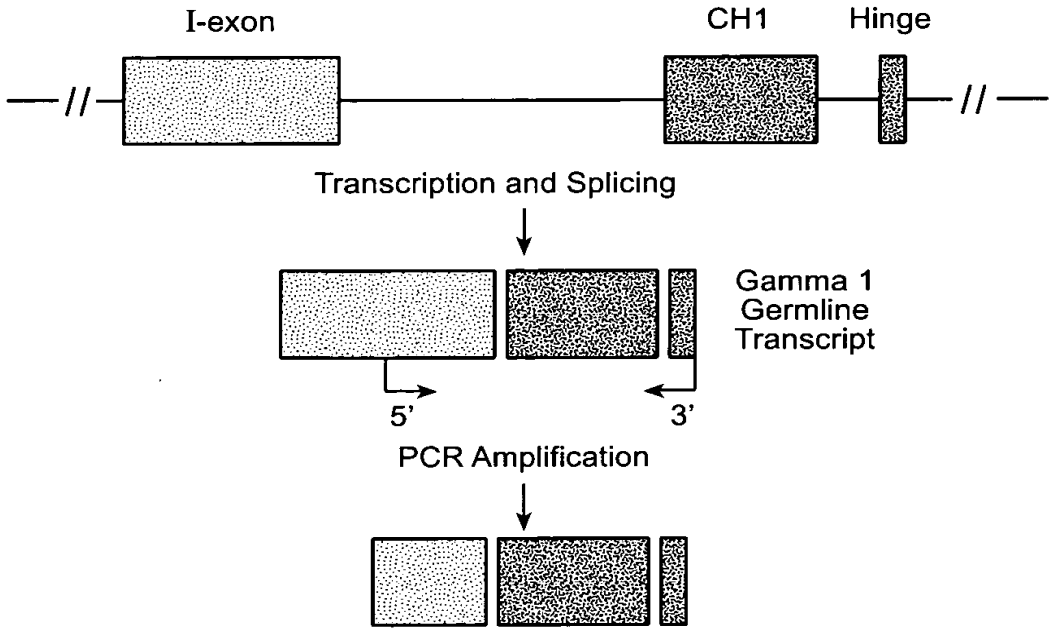
I-exon
CH1
Hinge
Transcription and Splicing
Gamma 1
Germline
Transcript
5'
3'
PCR Amplification
The Gamma 1 5' and 3' Primers amplify a completed probe of 370 BP

FIG._6

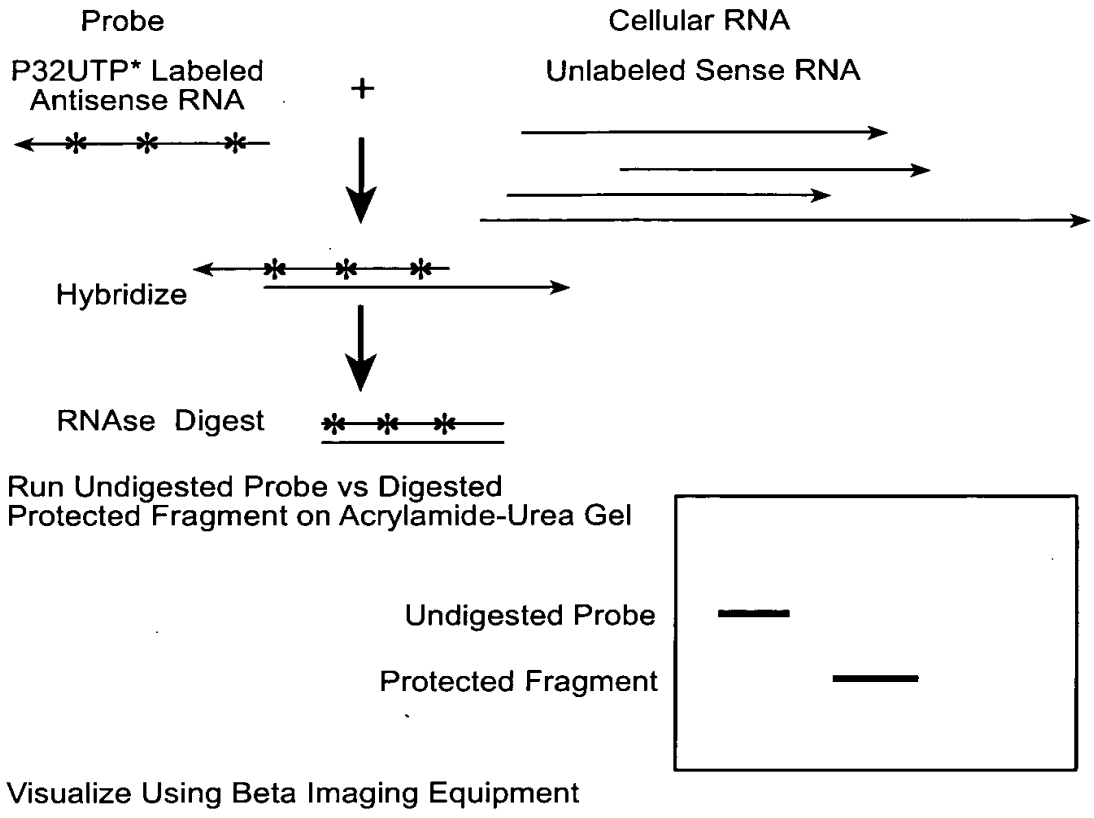

FIG._7

Alpha-1

L04541 = I Region Exon
BC005951 = Constant Region Exons

Alpha-2

L04541 = I Region Exon
AL389978 = Constant Region Exons

Epsilon

X56797= I Region Exon
J00222 = Constant Region Exons

Gamma-1

A2122127 = I Region Exon
Z17370 = Constant Region Exons

Gamma-2

U39934 = I Region Exon
J00230 = Constant Region Exons

Gamma-3

Al122127 = I Region Exon
X16110 = Constant Region Exons

Gamma-4

X56796 = I Region Exon
K01316 = Constant Region Exons

FIG._9

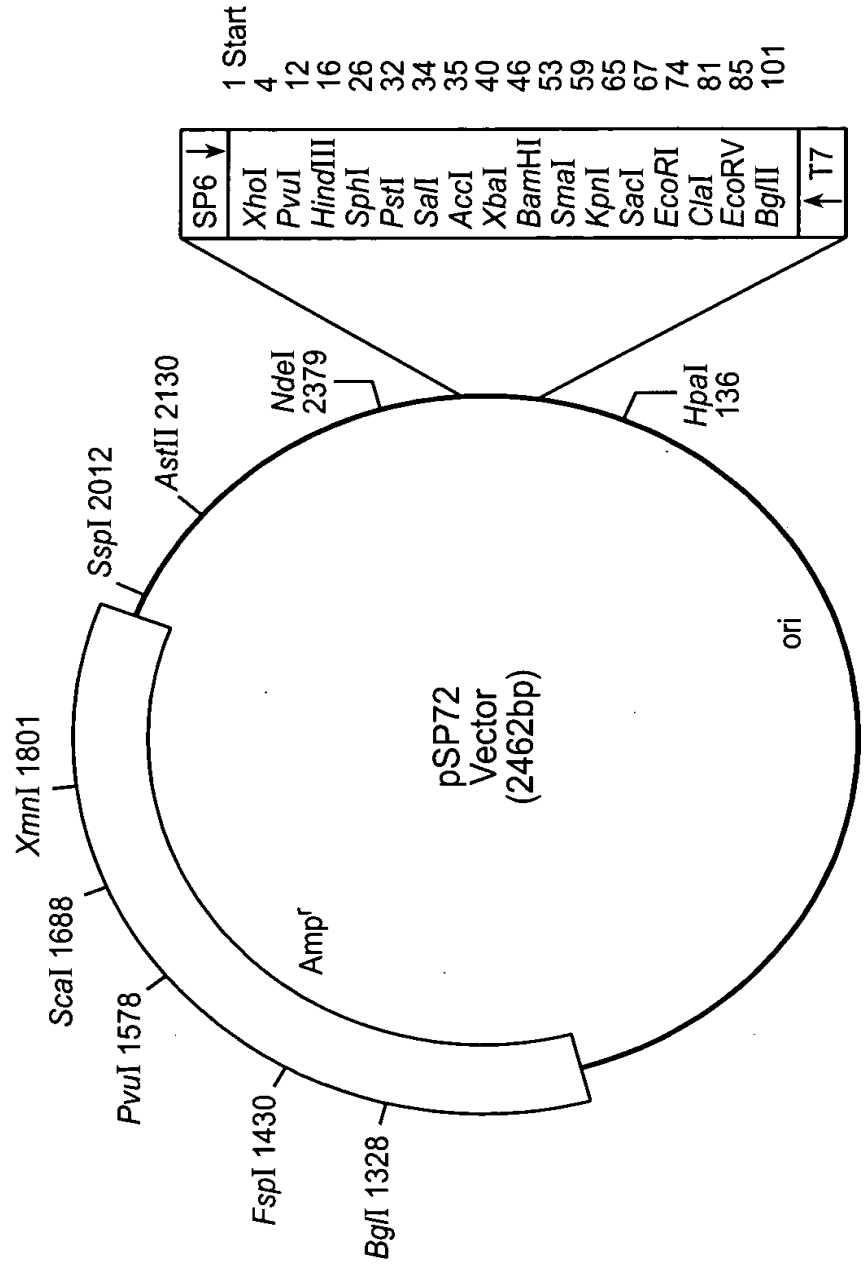
pSP72
Vector
(2462bp)
ori
Amp^r
SP6
XhoI
PvuI
HindIII
SphI
PstI
SalI
AccI
XbaI
BamHI
SmaI
KpnI
SacI
EcoRI
ClaI
EcoRV
BglII
T7
1 Start
4
12
16
26
32
34
35
40
46
53
59
65
67
74
81
85
101
NdeI 2379
HpaI 136
AstII 2130
SspI 2012
XmnI 1801
ScaI 1688
PvuI 1578
FspI 1430
BglI 1328

FIG._8